

What is claimed is:

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1. A compound of from 8 to 80 nucleobases in length targeted to a nucleic acid molecule encoding growth hormone receptor, wherein said compound specifically hybridizes with said nucleic acid molecule encoding growth hormone receptor (SEQ
10 ID NO: 4 or SEQ ID NO: 18) and inhibits the expression of growth hormone receptor.

2. A compound according to claim 1 which is from 12 to 50 nucleobases in length.

3. A compound according to claim 1 which is from 15 to
15 30 nucleobases in length.

4. A compound according to claim 1 comprising an oligonucleotide.

5. A compound according to claim 4 in which the oligonucleotide is an antisense oligonucleotide.

20 6. A compound according to claim 4 in which the oligonucleotide is a DNA oligonucleotide.

7. A compound according to claim 4 in which the oligonucleotide is a RNA oligonucleotide.

25 8. A compound according to claim 4 in which the oligonucleotide is a chimeric oligonucleotide.

9. A compound according to claim 7 which is a short interfering RNA (siRNA) molecule.

10. A compound according to claim 1 having at least 70% complementarity with the nucleic acid molecule encoding growth
30 hormone receptor (SEQ ID NO: 4 or SEQ ID NO: 18)

11. A compound according to claim 1 having at least 80% complementarity with the nucleic acid molecule encoding growth hormone receptor (SEQ ID NO: 4 or SEQ ID NO: 18).

12. A compound according to claim 1 having at least 90% complementarity with the nucleic acid molecule encoding growth hormone receptor (SEQ ID NO: 4 or SEQ ID NO: 18).

13. A compound according to claim 1 having at least 95% complementarity with the nucleic acid molecule encoding growth hormone receptor (SEQ ID NO: 4 or SEQ ID NO: 18).

14. A compound according to claim 1 which comprises at least an 8-nucleobase portion of SEQ ID NO: 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 73, 74, 75, 76, 77, 78, 79, 81, 82, 83, 84, 85, 86, 87, 88, 89, 91, 92, 93 or 94.

15. A compound according to claim 14 in which the oligonucleotide is selected from SEQ ID NOs: 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 73, 74, 75, 76, 77, 78, 79, 81, 82, 83, 84, 85, 86, 87, 88, 89, 91, 92, 93 and 94.

16. A compound according to claim 15 in which the oligonucleotide is selected from SEQ ID NOs: 30, 44 and 57.

17. A compound according to claim 1 in which the compound specifically hybridises with a region, encoding growth hormone receptor (SEQ ID NO: 4 or SEQ ID NO: 18), which region, segment or site comprises a translation initiation codon, a termination codon, a coding region, a 5' untranslated region, a 3' untranslated region, an intron:exon junction or an exon:intron junction.

18. A compound according to claim 17 in which the region, segment or site of the nucleic acid molecule comprises at least an 8-nucleobase portion of a sequence selected from SEQ ID NOs: 161-232.

19. A compound according to claim 1 which inhibits the expression of growth hormone receptor by at least 45%.

20. A compound according to claim 1 having at least one modified internucleoside linkage, sugar moiety, or nucleobase.

5 21. A compound according to claim 20 having at least one 2'-O-methoxyethyl sugar moiety.

22. A compound according to claim 20 having at least one phosphorothioate internucleoside linkage.

10 23. A compound according to claim 20 having at least one 5-methylcytosine.

24. A method of inhibiting the expression of growth hormone receptor in cells or tissues comprising contacting said cells or tissues with a compound according to claim 1.

15 25. A method of screening for a modulator of growth hormone receptor, the method comprising the steps of:

a) contacting a preferred target segment of a nucleic acid molecule encoding growth hormone receptor with one or more candidate modulators of growth hormone receptor, and

20 b) identifying one or more modulators of growth hormone receptor expression which modulate the expression of growth hormone receptor.

25 26. The method of claim 25 wherein the modulator of growth hormone receptor expression comprises an oligonucleotide, an antisense oligonucleotide, a DNA oligonucleotide, an RNA oligonucleotide, an RNA oligonucleotide having at least a portion of said RNA oligonucleotide capable of hybridizing with RNA to form an oligonucleotide-RNA duplex, or a chimeric oligonucleotide.

30 27. The method of claim 25 further comprising "benchmarking" the candidate modulator of growth hormone receptor relative to a known inhibitor of growth hormone receptor signaling, activity or expression or the growth hormone/insulin-like growth factor axis.

28. The method of claim 27 wherein the known inhibitor of growth hormone receptor signaling, activity or expression is a dopamine agonist, a somatostatin analog or growth hormone receptor antagonist.

5 29. The method of claim 28 wherein the known inhibitor of growth hormone receptor signaling, activity or expression is Trovert, octreotide, Sandostatin, bromocriptine mesylate or cabergoline or a compound of claim 1.

10 30. A diagnostic method for identifying a disease state comprising identifying the presence of growth hormone receptor in a sample using at least one of the primers comprising SEQ ID NOs 5 or 6, or the probe comprising SEQ ID NO 7.

31. A kit or assay device comprising the compound of claim 1.

15 32. A method of treating an animal having a disease or condition associated with growth hormone receptor signaling or the growth hormone/insulin-like growth factor axis comprising administering to said animal a therapeutically or prophylactically effective amount of an oligonucleotide capable
20 of modulating growth hormone receptor or insulin-like growth factor levels or expression.

33. A method according to claim 32 in which the oligonucleotide is a compound according to claim 1.

25 34. A method according to claim 32 in which the disease or condition is acromegaly, gigantism, cancer, diabetes, diabetic nephropathy, diabetic retinopathy, aberrant neovascularization, aberrant angiogenesis, macular degeneration, rheumatoid arthritis or shortened lifespan.

30 35. A method according to claim 32 in which the animal is a human.

36. A method of inhibiting the expression of insulin-like growth factor-1 in cells or tissues comprising contacting said cells or tissues with a compound according to claim 1 so that

expression of growth hormone receptor and insulin-like growth factor-1 are inhibited.

37. A method of screening for a modulator of growth hormone receptor signaling, the method comprising the steps of:

5 a) contacting a preferred target segment of a nucleic acid molecule encoding growth hormone receptor with one or more candidate modulators of growth hormone receptor, and

b) identifying one or more modulators of growth hormone receptor expression which modulate growth hormone receptor
10 signaling.

38. The method of claim 37 wherein the modulator of growth hormone receptor expression comprises an oligonucleotide, an antisense oligonucleotide, a DNA oligonucleotide, an RNA oligonucleotide, an RNA oligonucleotide having at least a
15 portion of said RNA oligonucleotide capable of hybridizing with RNA to form an oligonucleotide-RNA duplex, or a chimeric oligonucleotide.

39. The method of claim 37 wherein the modulator of growth hormone receptor expression modulates insulin-like growth
20 factor-1 expression.

40. The method of claim 37 further comprising "benchmarking" the candidate modulator of growth hormone receptor relative to a known inhibitor of growth hormone receptor signaling, activity or expression or the growth
25 hormone/insulin-like growth factor axis.

41. The method of claim 40 wherein the known inhibitor of growth hormone receptor signaling, activity or expression is a dopamine agonist, a somatostatin analog or growth hormone receptor antagonist.

30 42. The method of claim 41 wherein the known inhibitor of growth hormone receptor signaling, activity or expression is Trovert, octreotide, Sandostatin, bromocriptine mesylate or cabergoline or a compound of claim 1.

43. Use of a compound targeted to a nucleic acid molecule encoding growth hormone receptor in the manufacture of a medicament for the treatment of a disease or condition associated with growth hormone receptor signaling.

5 44. The use according to claim 43 wherein the compound targeted to a nucleic acid molecule encoding growth hormone receptor is an antisense oligonucleotide targeted to a nucleic acid molecule encoding growth hormone.

10 45. The use according to claim 43 wherein the disease or condition is acromegaly, gigantism, cancer, diabetes, diabetic nephropathy, diabetic retinopathy, aberrant neovascularization, aberrant angiogenesis, macular degeneration, rheumatoid arthritis or shortened lifespan.